Search Strategy

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FILE 'USPATFULL' ENTERED AT 20:46:35 ON 09 DEC 2003

E MOSS RONALD B/IN
L1 9 S E2-E5 E CARLO DENNIS J/IN
L2 36 S E3
L3 11 S L2 AND (HIV OR HUMAN IMMUNODEFICIENCY VIRUS)
L4 29456 S (HIV OR HUMAN IMMUNODEFICIENCY VIRUS)
L5 214 S L4 AND (REMUNE)
L6 1 S L5 AND REMUNE/CLM
L7 213 S L5 AND ANTIVIRAL?
L8 33 S L7 AND AY<2001
L9 2 S L7 AND (IMMUNIZ?/CLM OR VACCIN?/CLM)

FILE 'WPIDS' ENTERED AT 21:04:31 ON 09 DEC 2003

E MOSS RONALD B/IN E MOSS R B/IN
L10 3 S E3 E CARLO D J/IN
L11 32 S E3
L12 3 S L11 AND (HIV OR HUMAN IMMUNODEFICIENCY VIRUS)
L13 16878 S (HIV OR HUMAN IMMUNODEFICIENCY VIRUS)
L14 2407 S L13 AND ANTIVIRAL?
L15 0 S L14 AND REMUNE
L16 66 S L14 AND (VACCINATION OR IMMUNIZATION)

     FILE 'MEDLINE' ENTERED AT 21:44:31 ON 09 DEC 2003

L1       136279 S (HIV OR HUMAN IMMUNODEFICIENCY VIRUS)
L2        17611 S L1 AND (ANTIVIRAL? OR ANTIRETROVIRAL?)
L3          364 S L2 AND (VACCINATION OR IMMUNIZATION)
L4          206 S L3 AND PY<2001
                E CARLO D J/AU
L5           98 S E3-E5
L6          203 S L4 NOT L5
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2003:64308 Method for treating an HIV-infected individual by combining immunization with structured interruption of anti-retroviral treatment.
Moss, Ronald B., San Diego, CA, UNITED STATES
Carlo, Dennis J., Rancho Santa Fe, CA, UNITED STATES
US 2003044428 A1 20030306
APPLICATION: US 2002-56420 A1 20020124 (10)
PRIORITY: US 2001-264476P 20010126 (60)
DOCUMENT TYPE: Utility; APPLICATION.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The invention provides a method for the treatment of HIV infected individuals. The method is practiced by combining immunization with an HIV immunogenic composition with structured cycles of anti-retroviral treatment and withdrawal from treatment.

CLM What is claimed is:

1. A method of treating an HIV-infected individual, comprising: (a) treating an HIV-infected individual with at least one anti-retroviral compound; (b) immunizing said individual with an HIV immunogenic composition; (c) withdrawing treatment with said anti-retroviral compound; (d) reinitiating treatment with at least one anti-retroviral compound; (e) repeating step (c) at least once; and (f) optionally repeating step (d) at least once.

2. The method of claim 1, wherein said immunization induces an anti-HIV CD4+ T helper cell response.

3. The method of claim 1, wherein said immunization comprises administering said HIV immunogenic composition more than once.

4. The method of claim 1, wherein said HIV immunogenic composition comprises a whole-killed HIV virus devoid of outer envelope protein gp120.

5. The method of claim 1, wherein said HIV immunogenic composition comprises an adjuvant.

6. The method of claim 5, wherein said adjuvant comprises incomplete Freund's adjuvant

7. The method of claim 1, wherein said HIV immunogenic composition comprises at least one immunostimulatory sequence (ISS).

8. The method of claim 1, wherein said HIV immunogenic composition is REMUNE.TM..

9. The method of claim 1, wherein said HIV immunogenic composition is a combination of REMUNE.TM. and at least one ISS.

10. The method of claim 1, wherein said anti-retroviral compound is selected from the group consisting of a protease inhibitor, a reverse transcriptase inhibitor and a ribonucleotide reductase inhibitor.

11. The method of claim 1, wherein said anti-retroviral compound is selected from the group consisting of a viral adsorption inhibitor, an HIV entry inhibitor, an integrase inhibitor and a virus-cell fusion inhibitor.

12. The method of claim 1, wherein said anti-retroviral treatment in step (a) reduces HIV viral load to less than 5000 copies/ml.

13. The method of claim 1, wherein said anti-retroviral treatment in step (a) reduces HIV viral load to less than 500 copies/ml.

14. The method of claim 1, wherein said anti-retroviral treatment in step (a) reduces HIV viral load to less than 50 copies/ml.

15. The method of claim 1, wherein said withdrawal in step (c) is for a period of time until viral load rises to greater than about 100,000 copies/ml.

16. The method of claim 1, wherein said withdrawal in step (c) is for a period of time until viral load rises to greater than about 50,000 copies/ml.

17. The method of claim 1, wherein said withdrawal in step (c) is for a period of time until viral load rises to greater than about 20,000 copies/ml.

18. The method of claim 1, wherein said withdrawal in step (c) is for a period of at least 2 weeks.

19. The method of claim 1, wherein said withdrawal in step (c) is for a period of about 8 weeks.

20. The method of claim 1, wherein reinitiating said anti-retroviral treatment in step (d) reduces HIV viral load to less than 5000 copies/ml.

21. The method of claim 1, wherein reinitiating said anti-retroviral treatment in step (d) reduces HIV viral load to less than 500 copies/ml.

22. The method of claim 1, wherein reinitiating said anti-retroviral treatment in step (d) reduces HIV viral load to less than 50 copies/ml.

23. The method of claim 1, wherein said reinitiated anti-retroviral treatment in step (d) is for a period of about 8 weeks.

24. The method of claim 1, wherein HIV viral load in said individual following step (e) is maintained at less than about 10,000 copies/ml for a period of at least about 8 weeks.

25. The method of claim 1, wherein HIV viral load in said individual following step (e) is maintained at less than about 5,000 copies/ml for a period of at least about 8 weeks.

26. The method of claim 1, wherein HIV viral load in said individual following step (e) is maintained at less than about 500 copies/ml for a period of at least about 8 weeks.

L3 ANSWER 5 OF 11 USPATFULL on STN

2000:9534 Prevention and treatment of retroviral disease.
Salk, Jonas, La Jolla, CA, United States
Carlo, Dennis J., Rancho Santa Fe, CA, United States
The Immune Response Corporation, Carlsbad, CA, United States (U.S. corporation)
US 6017543 20000125
APPLICATION: US 1995-467302 19950605 (8)
DOCUMENT TYPE: Utility; Granted.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention provides a non-infectious immunotherapeutic containing retroviral particles devoid of outer envelope proteins or containing selected antigens isolated from a retrovirus. There is also provided a vaccine effective against HIV. In one aspect, the immunogen is useful for immunizing an individual previously infected by a retrovirus including HIV, so as to induce immunoprotective factors protective against progression of the infection. In another aspect, the vaccine is useful for vaccinating an individual not previously infected with HIV in order to prevent subsequently acquired infection. In another aspect, there is provided a method of rendering a viral immunogen non-infectious. The immunogen may also be used to produce antibodies for passive immunotherapy, alone or in conjunction with active immunotherapy, in individuals infected with a retrovirus, including HIV, preferably those individuals exhibiting low levels of antibodies to retroviral gene products other than the outer envelope.

CLM What is claimed is:
1. A method of stimulating the immune system of a human to produce antibodies or maintain the level of CD4+ cells, comprising administering an immunogen comprising intact and inactivated HIV.

2. The method of claim 1, wherein said immunogen is administered in combination with an adjuvant.

3. The method of claim 1, wherein said human is immunocompetent.

4. A method of prolonging the survival of a human infected with HIV, comprising administering an immunogen comprising intact and inactivated HIV, wherein said administration of said immunogen stimulates the immune system of said human to produce antibodies or maintain the level of CD4+ cells.

5. The method of claim 1, wherein said human is infected with HIV.

6. The method of claim 1, wherein said human is not infected with HIV.

L3 ANSWER 6 OF 11 USPATFULL on STN

1999:85281 Prevention and treatment of retroviral disease.
Salk, Jonas, La Jolla, CA, United States
Carlo, Dennis J., Rancho Santa Fe, CA, United States
Immune Response Corporation, Carlsbad, CA, United States (U.S. corporation)
US 5928930 19990727
APPLICATION: US 1995-464137 19950605 (8)
DOCUMENT TYPE: Utility; Granted.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention provides a non-infectious immunotherapeutic containing retroviral particles devoid of outer envelope proteins or containing selected antigens isolated from a retrovirus. There is also provided a vaccine effective against HIV. In one aspect, the immunogen is useful for immunizing an individual previously infected by a retrovirus including HIV, so as to induce immunoprotective factors protective against progression of the infection. In another aspect, the vaccine is useful for vaccinating an individual not previously infected with HIV in order to prevent subsequently acquired infection. In another aspect, there is provided a method of rendering a viral immunogen non-infectious. The immunogen may also be used to produce antibodies for passive immunotherapy, alone or in conjunction with active immunotherapy, in individuals infected with a retrovirus,

including HIV, preferably those individuals exhibiting low levels of antibodies to retroviral gene products other than the outer envelope.

CLM What is claimed is:

1. A method of producing cell lines producing monoclonal antibodies useful for the treatment of HIV infections, comprising the steps of: a. obtaining cells immunized with an immunogen preparation comprising intact non-infectious HIV devoid of outer envelope proteins; and b. immortalizing said cells.

2. A method of producing cell lines producing monoclonal antibodies useful for the treatment of HIV infections, comprising the steps of: a. obtaining cells immunized with an immunogen preparation comprising two or more HIV proteins, with the proviso that none of said HIV proteins is an outer envelope protein; and b. immortalizing said cells.

3. Cell lines produced by the method of claim 1 or claim 2.

4. Monoclonal antibodies produced by the cell lines of claim 3.

5. A method of producing cell lines producing monoclonal antibodies useful for the treatment of HIV infections, comprising the steps of: a. obtaining antibody-producing cells from an individual infected with said HIV; b. selecting a cell producing an antibody reactive with the immunogen preparation of claim 1 or claim 2; and c. immortalizing said cell.

6. Cell lines produced by the method of claim 5.

7. Monoclonal antibodies produced by the cell lines of claim 6.

8. A composition, comprising the immunogen preparation of claim 2.

9. A method of obtaining immunoglobulins useful for the treatment of HIV infections, comprising the steps of: a. selecting an individual having an HIV infection and exhibiting immunocompetence; b. recovering immunoglobulins from said individual; and c. purifying said immunoglobulins.

10. The method of claim 9, further comprising removing anti-gp160/120 antibodies from said recovered immunoglobulins.

11. A method of producing cell lines producing monoclonal antibodies useful for the treatment of retroviral infections, comprising the steps of: a. obtaining cells immunized with an immunogen preparation comprising two or more retroviral proteins, with the proviso that none of said retroviral proteins is an outer envelope protein; and b. immortalizing said cells.

12. Cell lines produced by the method of claim 11.

13. Monoclonal antibodies produced by the cell lines of claim 12.

14. A method of producing cell lines producing monoclonal antibodies useful for the treatment of retroviral infections, comprising the steps of: a. obtaining antibody-producing cells from an individual infected with said retrovirus; b. selecting a cell producing an antibody reactive with an immunogen preparation comprising two or more retroviral proteins, with the proviso that none of said retroviral proteins is an outer envelope protein; and c. immortalizing said cell.

15. Cell lines produced by the method of claim 14.

16. Monoclonal antibodies produced by the cell lines of claim 15.

17. A composition, comprising an immunogen comprising two or more retroviral proteins, with the proviso that none of said retroviral proteins is an outer envelope protein.

L3 ANSWER 7 OF 11 USPATFULL on STN

1999:72499 Prevention and treatment of retroviral disease.
Salk, Jonas, La Jolla, CA, United States
Carlo, Dennis J., Rancho Santa Fe, CA, United States
The Immune Response Corporation, Carlsbad, CA, United States (U.S. corporation)
US 5916806 19990629
APPLICATION: US 1995-464139 19950605 (8)
DOCUMENT TYPE: Utility; Granted.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention provides a non-infectious immunotherapeutic containing retroviral particles devoid of outer envelope proteins or containing selected antigens isolated from a retrovirus. There is also provided a vaccine effective against HIV. In one aspect, the immunogen is useful for immunizing an individual previously infected by a retrovirus including HIV, so as to induce immunoprotective factors protective against progression of the infection. In another aspect, the vaccine is useful for vaccinating an individual not previously infected with HIV in order to prevent subsequently acquired infection. In another aspect, there is provided a method of rendering a viral immunogen non-infectious. The immunogen may also be used to produce antibodies for passive immunotherapy, alone or in conjunction with active immunotherapy, in individuals infected with a retrovirus, including HIV, preferably those individuals exhibiting low levels of antibodies to retroviral gene products other than the outer envelope.

CLM What is claimed is:
1. A method of producing anti-retroviral antibodies, comprising the steps of: a) immunizing a mammal with an immunogen comprising intact non-infectious retrovirus devoid of outer envelope proteins, whereby said immunization stimulates production of anti-retroviral antibodies; and b) recovering the anti-retroviral antibodies produced by said mammal.

2. Purified and isolated anti-retroviral antibodies produced by the method of claim 1.

3. A method of producing anti-HIV antibodies, comprising the steps of: a) immunizing a mammal with an immunogen comprising intact non-infectious HIV devoid of outer envelope proteins, whereby said immunization stimulates production of anti-HIV antibodies; and b) recovering the anti-HIV antibodies produced by said mammal.

4. Purified and isolated anti-HIV antibodies produced by the method of claim 3.

5. A method of producing cell lines producing monoclonal antibodies useful for the treatment of retroviral infections, comprising the steps of: a. obtaining cells immunized with an immunogen comprising intact non-infectious retrovirus devoid of outer envelope proteins; and b.

immortalizing said cells.

6. Cell lines produced by the method of claim 5.

7. Monoclonal antibodies produced by the cell lines of claim 6.

8. A method of producing cell lines producing monoclonal antibodies useful for the treatment of retroviral infections, comprising the steps of: a. obtaining antibody-producing cells from an individual infected with said retrovirus; b. selecting a cell producing an antibody reactive with an immunogen comprising intact non-infectious retrovirus devoid of outer envelope proteins; and c. immortalizing said cell.

9. Cell lines produced by the method of claim 8.

10. Monoclonal antibodies produced by the cell lines of claim 9.

L3 ANSWER 8 OF 11 USPATFULL on STN

1999:48097 Prevention and treatment of retroviral disease.
Salk, Jonas, La Jolla, CA, United States
Carlo, Dennis J., Rancho Santa Fe, CA, United States
The Immune Response Corporation, Carlsbad, CA, United States (U.S. corporation)
US 5895650 19990420
APPLICATION: US 1995-467334 19950605 (8)
DOCUMENT TYPE: Utility; Granted.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention provides a non-infectious immunotherapeutic containing retroviral particles devoid of outer envelope proteins or containing selected antigens isolated from a retrovirus. There is also provided a vaccine effective against HIV. In one aspect, the immunogen is useful for immunizing an individual previously infected by a retrovirus including HIV, so as to induce immunoprotective factors protective against progression of the infection. In another aspect, the vaccine is useful for vaccinating an individual not previously infected with HIV in order to prevent subsequently acquired infection. In another aspect, there is provided a method of rendering a viral immunogen non-infectious. The immunogen may also be used to produce is antibodies for passive immunotherapy, alone or in conjunction with active immunotherapy, in individuals infected with a retrovirus, including HIV, preferably those individuals exhibiting low levels of antibodies to retroviral gene products other than the outer envelope.

CLM What is claimed is:
1. A method of stimulating the immune system of a human having a retrovirus infection to produce antibodies or maintain the level of CD4+ cells, comprising administering an immunogen comprising a non-infectious preparation of said retrovirus.

2. A method of preparing a non-infectious viral immunogen for use in a physiologically acceptable solution, comprising treating a virus with beta propiolactone and gamma radiation.

3. A non-infectious immunogen prepared by the method of claim 2.

4. An immunogen comprising whole inactivated retroviral particles in a physiologically acceptable solution.

5. An immunogen comprising whole inactivated HIV particles in a physiologically acceptable solution.

6. The immunogen of claim 4 or 5, wherein said retroviral particles are rendered inactive by treatment with gamma radiation and beta-propiolactone.

7. The immunogen of claim 4 or 5, further comprising an adjuvant.

L3 ANSWER 9 OF 11 USPATFULL on STN

1999:36710 Prevention and treatment of retroviral disease.
Salk, Jonas, La Jolla, CA, United States
Carlo, Dennis J., Rancho Santa Fe, CA, United States
The Immune Response Corporation, Carlsbad, CA, United States (U.S. corporation)
US 5885578 19990323
APPLICATION: US 1995-469739 19950605 (8)
DOCUMENT TYPE: Utility; Granted.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention provides a non-infectious immunotherapeutic containing retroviral particles devoid of outer envelope proteins or containing selected antigens isolated from a retrovirus. There is also provided a vaccine effective against HIV. In one aspect, the immunogen is useful for immunizing an individual previously infected by a retrovirus including HIV, so as to induce immunoprotective factors protective against progression of the infection. In another aspect, the vaccine is useful for vaccinating an individual not previously infected with HIV in order to prevent subsequently acquired infection. In another aspect, there is provided a method of rendering a viral immunogen non-infectious. The immunogen may also be used to produce antibodies for passive immunotherapy, alone or in conjunction with active immunotherapy, in individuals infected with a retrovirus, including HIV, preferably those individuals exhibiting low levels of antibodies to retroviral gene products other than the outer envelope.

CLM What is claimed is:
1. A method of producing anti-HIV antibodies, comprising the steps of: a) immunizing a mammal with an immunogen comprising two or more HIV proteins, provided that none of said HIV proteins is an outer envelope protein, whereby said immunization stimulates production of anti-HIV antibodies; and b) recovering the anti-HIV antibodies produced by said mammal.

2. Purified and isolated anti-HIV antibodies produced by the method of claim 1.

3. A method of obtaining anti-retroviral antibodies, comprising the steps of: a) selecting an immunocompetent individual having a retroviral infection; and b) recovering anti-retroviral antibodies produced by said individual.

4. Purified and isolated anti-retroviral antibodies obtained by the method of claim 3.

5. A method of obtaining anti-HIV antibodies, comprising the steps of: a) selecting an immunocompetent individual having an HIV infection; and b) recovering anti-HIV antibodies produced by said individual.

6. Purified and isolated anti-HIV antibodies obtained by the method of claim 5.

7. A method of producing anti-retroviral antibodies, comprising the steps of: a) immunizing a mammal with an immunogen comprising two or more retroviral proteins, provided that none of said retroviral proteins is an outer envelope protein, whereby said immunization stimulates production of anti-retroviral antibodies; and b) recovering the anti-retroviral antibodies produced by said mammal.

8. Purified and isolated anti-retroviral antibodies produced by the method of claim 7.

9. An immunogen comprising a non-infectious intact retrovirus devoid of outer envelope proteins.

10. The immunogen of claim 9, wherein said retrovirus is rendered non-infectious by treatment with gamma radiation and beta-propriolactone.

11. A composition comprising the immunogen of claim 9 together with an adjuvant.

12. A method of preparing the immunogen of claim 9, comprising the steps of: a. growing intact retrovirus in culture; and b. removing the outer envelope proteins from said intact retrovirus.

13. A method of producing antibodies useful for the treatment of retroviral infections, comprising the steps of: a. immunizing a mammal with the immunogen of claim 9; and b. recovering the antibodies produced by said mammal.

14. Isolated antibodies produced by the method of claim 13.

L3 ANSWER 10 OF 11 USPATFULL on STN

1998:162001 Prevention and treatment of retroviral disease.
Salk, Jonas, La Jolla, CA, United States
Carlo, Dennis J., Rancho Santa Fe, CA, United States
The Immune Response Corporation, Carlsbad, CA, United States (U.S. corporation)
US 5853725 19981229
APPLICATION: US 1994-233508 19940426 (8)
DOCUMENT TYPE: Utility; Granted.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention provides a non-infectious immunotherapeutic containing retroviral particles devoid of outer envelope proteins or containing selected antigens isolated from a retrovirus. In one aspect, the immunogen is useful for immunizing an individual previously infected by a retrovirus including HIV, so as to induce factors against progression of the infection. In another aspect, there is provided a method of rendering a viral immunogen non-infectious. The immunogen may also be used to produce antibodies for passive immunotherapy, alone or in conjunction with active immunotherapy, in individuals infected with a retrovirus, including HIV, preferably those individuals exhibiting low levels of antibodies to retroviral gene products other than the outer envelope.

CLM What is claimed is:

1. A method of stimulating the immune system of a human to produce antibodies, reduce viral burden or maintain CD4+ levels, comprising administering an immunogen comprising non-infectious intact HIV devoid of outer envelope proteins.

2. The method of claim 1, wherein the immunogen is administered with an adjuvant.

3. The method of claim 1, wherein the immunogen is administered without an adjuvant.

4. The method of claim 1, wherein said human is infected with HIV.

5. The method of claim 1, wherein said human is not infected with HIV.

6. A method of stimulating the immune system of a human to produce antibodies, reduce viral burden or maintain CD4+ levels, comprising administering an immunogen comprising two or more HIV proteins, provided that none of said HIV proteins is an outer envelope protein.

7. The method of claim 6, wherein the immunogen is administered with an adjuvant.

8. The method of claim 6, wherein the immunogen is administered without an adjuvant.

9. The method of claim 6, wherein said human is infected with HIV.

10. The method of claim 6, wherein said human is not infected with HIV.

11. A method of stimulating the immune system of a human to produce antibodies, reduce viral burden or maintain CD4+ levels, comprising administering an immunogen comprising non-infectious intact retrovirus devoid of outer envelope proteins.

12. The method of claim 11, wherein the immunogen is administered with an adjuvant.

13. The method of claim 11, wherein the immunogen is administered without an adjuvant.

14. The method of claim 11, wherein said human is infected with retrovirus.

15. The method of claim 11, wherein said human is not infected with retrovirus.

16. A method of stimulating the immune system of a human to produce antibodies, reduce viral burden or maintain CD4+ levels, comprising administering an immunogen comprising two or more retroviral proteins, provided that none of said retroviral proteins is an outer envelope protein.

17. The method of claim 16, wherein the immunogen is administered with an adjuvant.

18. The method of claim 16, wherein the immunogen is administered without an adjuvant.

19. The method of claim 16, wherein said human is infected with retrovirus.

20. The method of claim 16, wherein said human is not infected with retrovirus.

L3 ANSWER 11 OF 11 USPATFULL on STN

93:89774 Retroviral antigens.
Salk, Jonas, La Jolla, CA, United States
Carlo, Dennis J., Rancho Santa Fe, CA, United States
The Immune Response Corporation, Carlsbad, CA, United States (U.S. corporation)
US 5256767 19931026
APPLICATION: US 1992-975899 19921110 (7)
DOCUMENT TYPE: Utility; Granted.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention provides a non-infectious immunotherapeutic containing retroviral particles devoid of outer envelope proteins or containing selected antigens isolated from a retrovirus. There is also provided a vaccine effective against HIV. In one aspect, the immunogen is useful for immunizing an individual previously infected by a retrovirus including HIV, so as to induce immunoprotective factors protective against progression of the infection. In another aspect, the vaccine is useful for vaccinating an individual not previously infected with HIV in order to prevent subsequently acquired infection. In another aspect, there is provided a method of rendering a viral immunogen non-infectious. The immunogen may also be used to produce antibodies for passive immunotherapy, alone or in conjunction with active immunotherapy, in individuals infected with a retrovirus, including HIV, preferably those individuals exhibiting low levels of antibodies to retroviral gene products other than the outer envelope.

CLM What is claimed is:
1. An immunogen comprising a non-infectious intact HIV virus devoid of outer envelope proteins.

2. The immunogen of claim 1 wherein said outer envelope proteins are gp160 AND gp120.

3. An immunogen of claim 1, wherein said non-infectious intact HIV virus is rendered non-infectious by treatment with gamma radiation and beta-propiolactone.

4. A composition comprising the immunogen of claim 1 together with an adjuvant.

5. A method of preparing the immunogen of claim 1 comprising the steps of: a. growing the intact HIV virus in culture; and b. removing the outer envelope proteins from said intact HIV virus and recovering the immunogen.

6. A method of producing antibodies useful for the treatment of HIV infections, comprising the steps of: a. immunizing a mammal with the immunogen of claim 1; and b. recovering the antibodies produced by said mammal.

7. Isolated antibodies produced by the method of claim 6.

L10 ANSWER 1 OF 3 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN

AN 2002-643331 [69] WPIDS
DNC C2002-181653
TI Treating an HIV-infected individual comprises treatment with anti-retroviral compound and immunization with an HIV immunogenic composition with structured cycles of anti-retroviral treatment and withdrawal from treatment.
DC B04 D16
IN CARLO, D J; MOSS, R B
PA (CARL-I) CARLO D J; (MOSS-I) MOSS R B; (IMMU-N) IMMUNE RESPONSE CORP
CYC 101
PI WO 2002058726 A1 20020801 (200269)* EN 31p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG US UZ VN YU ZA ZM ZW
US 2003044428 A1 20030306 (200320)
EP 1355663 A1 20031029 (200379) EN
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI TR
ADT WO 2002058726 A1 WO 2002-US2077 20020124; US 2003044428 A1 Provisional US 2001-264476P 20010126, US 2002-56420 20020124; EP 1355663 A1 EP 2002-705944 20020124, WO 2002-US2077 20020124
FDT EP 1355663 A1 Based on WO 2002058726
PRAI US 2001-264476P 20010126; US 2002-56420 20020124

AB WO 200258726 A UPAB: 20021026
NOVELTY - Treating an HIV-infected individual comprises combining immunization with an anti-retroviral compound, an HIV immunogenic composition with structured cycles of anti-retroviral treatment and withdrawal from treatment.

DETAILED DESCRIPTION - A method for treating HIV comprises

(a) treating an HIV-infected individual with at least one anti-retroviral compound;

(b) immunizing the infected individual with an HIV immunogenic composition;

(c) withdrawing treatment with the anti-retroviral compound;

(d) reinitiating treatment with at least one anti-retroviral compound;

(e) repeating step (c) at least once; and

(f) optionally repeating step (d) at least once.

ACTIVITY - Anti-HIV.

The 8 chronically HIV-infected patients who were immunized with REMUNE were placed on a protocol in which HAART was withdrawn for a maximum of 8 weeks. During the first structured treatment interruption (STI), 3/8 REMUNE treated patients displayed viral load (VL) peaks of less than 10000 copies/ml. Then the patients were placed back on HAART for another 8 weeks. With immune activation of CD4 cells by immunization, and CD8 cells by autologous virus in combination with CD4 helper, further immune control, with a mean follow up of 7.5 weeks off HAART, was then realized during the second STI. 5 out of 8 of the REMUNE treated patients obtained virological peaks of less than 10000 copies/ml. 5 out of 8 patients decreased their viral load from the peak viral load during the second STI. The Least Squares slope suggested that baseline post-immunization p24 lymphocyte proliferative responses (LPRs) predicted the decrease in viral load peaks between the first and second STIs. The

patient with the lowest T helper baseline LPR to p24 antigen induced by immunization had the least control of viral replication.

MECHANISM OF ACTION - Protease-Inhibitor; Reverse-Transcriptase-Inhibitor; Ribonucleotide-Reductase-Inhibitor; Viral-Adsorption-Inhibitor; HIV-Entry-Inhibitor; Integrase-Inhibitor; Virus-Cell-Fusion-Inhibitor; Vaccine.

USE - The method is useful for treating an HIV-infected individual (claimed).

ADVANTAGE - The advantages of the method of the invention include

(1) a delay in the rebound to an unacceptably high viral load;

(2) a more rapid or sustained increase in HIV-specific CD4 T cell counts;

(3) a reduction or delay in the development of AIDS symptoms, including AIDS-related opportunistic infections;

(4) a higher degree of patient compliance with treatment and fewer toxic side effects associated with long-term anti-retroviral drug treatment; or

(5) a lower cost of treatment or percentage of patients developing drug resistant strains of virus.

Dwg.0/0

L10 ANSWER 2 OF 3 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN

AN 2001-031804 [04] WPIDS
DNC C2001-009690
TI Human immunodeficiency virus (HIV) compositions useful for immunizing and inhibiting AIDS in mammals, comprises HIV devoid of outer envelope protein and an immunostimulatory nucleic acid sequence.
DC B04
IN MOSS, R B
PA (IMMU-N) IMMUNE RESPONSE CORP
CYC 91
PI WO 2000067787 A2 20001116 (200104)* EN 64p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2000049929 A 20001121 (200112)
BR 2000010323 A 20020108 (200208)
EP 1176978 A2 20020206 (200218) EN
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI
ZA 2001008559 A 20020828 (200264) 85p
MX 2001010784 A1 20020301 (200362)
ADT WO 2000067787 A2 WO 2000-US12495 20000505; AU 2000049929 A AU 2000-49929 20000505; BR 2000010323 A BR 2000-10323 20000505, WO 2000-US12495 20000505; EP 1176978 A2 EP 2000-932163 20000505, WO 2000-US12495 20000505; ZA 2001008559 A ZA 2001-8559 20011018; MX 2001010784 A1 WO 2000-US12495 20000505, MX 2001-10784 20011024
FDT AU 2000049929 A Based on WO 2000067787; BR 2000010323 A Based on WO 2000067787; EP 1176978 A2 Based on WO 2000067787; MX 2001010784 A1 Based on WO 2000067787
PRAI US 1999-150667P 19990825; US 1999-132762P 19990506

AB WO 200067787 A UPAB: 20021105
NOVELTY - An immunogenic composition (I), comprising a whole-killed human immunodeficiency virus (HIV) devoid of outer envelope protein gp120, an isolated nucleic acid molecule containing an immunostimulatory sequence (ISS) and an adjuvant, which enhances beta -chemokine levels in a mammal,

is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) a kit comprising (I); and

(2) making (I), comprising combining a whole-killed HIV virus devoid of outer envelope protein gp120, an isolated nucleic acid molecule containing an immunostimulatory sequence (ISS) and an adjuvant.

ACTIVITY - Anti-HIV. The effect of immunogenic compositions containing an HIV antigen, an isolated nucleic acid molecule containing an ISS and an adjuvant in enhancing HIV-specific immune response was tested in primates. Three baboon fetuses were injected in utero with an immunogenic composition containing gp120-depleted HIV-1 (100 micro g total protein) in IFA with 500 micro g of the ISS having a sequence 5'-TCGTCGCTGTTGTCGTTTCTT-3'. Four weeks later, the fetuses were boosted using the same regimen. Peripheral blood mononuclear cells from the neonatal baboons were collected and proliferative responses to p24 and HIV-1 antigen were assayed. In all three animals, the HIV-1 stimulation index, which is the ratio of the T cell proliferation in response to antigen to T cell proliferation without antigen, was indicative of a strong immune response. Production of HIV-specific antibodies, cytokines and beta -chemokines were also measured in the same baboons. These results demonstrated that the HIV immunogenic compositions were effective in primates in stimulating HIV-specific immune responses. Furthermore, these results demonstrated that fetuses and infants were able to elicit strong HIV immune responses to the immunogenic compositions, indicating that these compositions are useful for preventing maternal transmission of HIV and as pediatric vaccines.

MECHANISM OF ACTION - Prevents initial infection of an individual exposed to HIV.

USE - (I) is useful for immunizing and for inhibiting AIDS in a mammal. The mammal can be a primate such as a human, (HIV seronegative or seropositive humans) or a rodent, in particular the primate is a pregnant mother or an infant (claimed).

ADVANTAGE - (I) can induce potent Th1 immune responses against a broad spectrum of HIV epitopes and provides a strong HIV-specific cytotoxic T lymphocyte response.

DESCRIPTION OF DRAWING(S) - The figure shows control and antigen-stimulated interferon- gamma (IFN- gamma) production for the indicated treatment groups.

Dwg.1/7

L12 ANSWER 3 OF 3 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN

AN 1988-368523 [51] WPIDS
DNC C1988-163115
TI Prevention and treatment of retroviral disease, esp. HIV - using immune methods and agents e.g. retroviral particles devoid of outer envelope protein.
DC B04 D16 P34
IN CARLO, D J; SALK, J
PA (IMMU-N) IMMUNE RESPONSE CORP; (IMMU-N) IMMUNE RESPONSE CORP INC; (IMMU-N) IMMUNE RESPONSE COR
CYC 24
PI WO 8809670 A 19881215 (198851)* EN 28p
RW: AT BE CH DE FR GB IT LI LU NL OA SE
W: AU BR DK FI JP NO SD SU
AU 8819626 A 19890104 (198919)
NO 8900565 A 19890410 (198920)
EP 317622 A 19890531 (198922) EN
R: AT BE CH DE FR GB IT LI LU NL OA SE
DK 8900563 A 19890208 (198926)

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      FI 8900603    A  19890208 (198940)
      JP 02500440   W  19900215 (199013)
      IL 86675      A  19930404 (199318)
      US 5256767    A  19931026 (199344)        10p
      EP 602761     A1 19940622 (199424)  EN    13p
          R: AT BE CH DE FR GB IT LI LU NL SE
      IL 104337     A  19940530 (199424)
      IL 104340     A  19940624 (199427)
      NO 175846     B  19940912 (199436)
      IL 104339     A  19950124 (199510)
      EP 317622     A4 19900704 (199512)
      JP 07020880   B2 19950308 (199514)         9p
      SU 1837890    A1 19930830 (199519)         8p
      CA 1336407    C  19950725 (199537)
      EP 685236     A1 19951206 (199602)  EN    13p
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      FI 95871      B  19951229 (199605)
      EP 317622     B1 19960103 (199606)  EN    12p
          R: AT BE CH DE FR GB IT LI LU NL SE
      IL 104338     A  19951127 (199608)
      DE 3854857    G  19960215 (199612)
      BR 1101124    A3 19981110 (199850)#
      RU 2111010    C1 19980520 (199850)
      US 5853725    A  19981229 (199908)
      US 5885578    A  19990323 (199919)
      US 5895650    A  19990420 (199923)
      US 5916806    A  19990629 (199932)
      US 5928930    A  19990727 (199936)
      US 6017543    A  20000125 (200012)
ADT   WO 8809670 A WO 1988-US1955 19880609; EP 317622 A EP 1988-906347 19880609;
      JP 02500440 W JP 1988-505484 19880609; IL 86675 A IL 1988-86675 19880609;
      US 5256767 A CIP of US 1987-60280 19870610, Cont of US 1988-200752
      19880531, US 1992-975899 19921110; EP 602761 A1 Related to EP 1988-906347
      19880609, EP 1993-250368 19880609; IL 104337 A IL 1988-104337 19880609; IL
      104340 A IL 1988-104340 19880609; NO 175846 B WO 1988-US1955 19880609, NO
      1989-565 19890209; IL 104339 A IL 1988-104339 19880609; EP 317622 A4 EP
      1988-906347          ; JP 07020880 B2 JP 1988-505484 19880609, WO
      1988-US1955 19880609; SU 1837890 A1 WO 1988-US1955 19880609, SU
      1989-4613460 19890208; CA 1336407 C CA 1988-569026 19880609; EP 685236 A1
      EP 1995-250152 19880609; FI 95871 B WO 1988-US1955 19880609, FI 1989-603
      19890208; EP 317622 B1 EP 1988-906347 19880609, WO 1988-US1955 19880609;
      IL 104338 A IL 1988-104338 19880609; DE 3854857 G DE 1988-3854857
      19880609, EP 1988-906347 19880609, WO 1988-US1955 19880609; BR 1101124 A3
      BR 1997-1101124 19970514; RU 2111010 C1 SU 1988-5052305 19880609; US
      5853725 A CIP of US 1987-60280 19870610, Cont of US 1988-200752 19880531,
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      1988-200752 19880531, Cont of US 1992-975899 19921110, Cont of US
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      19950605; US 5916806 A CIP of US 1987-60280 19870610, Cont of US
      1988-200752 19880531, Cont of US 1992-975899 19921110, Cont of US
      1993-121318 19930915, Div ex US 1994-233508 19940426, US 1995-464139
      19950605; US 5928930 A CIP of US 1987-60280 19870610, Cont of US
      1988-200752 19880531, Cont of US 1992-975899 19921110, Cont of US
      1993-121318 19930915, Div ex US 1994-233508 19940426, US 1995-464137
      19950605; US 6017543 A CIP of US 1987-60280 19870610, Cont of US
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      1993-121318 19930915, Div ex US 1994-233508 19940426, US 1995-467302
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19950605
FDT IL 104337 A Div ex IL 86675; IL 104340 A Div ex IL 86675; NO 175846 B Previous Publ. NO 8900565; IL 104339 A Div ex IL 86675; JP 07020880 B2 Based on JP 02500440, Based on WO 8809670; FI 95871 B Previous Publ. FI 8900603; EP 317622 B1 Based on WO 8809670; IL 104338 A Div ex IL 86675; DE 3854857 G Based on EP 317622, Based on WO 8809670; US 5853725 A Cont of US 5256767; US 5885578 A Cont of US 5256767; US 5895650 A Cont of US 5256767; US 5916806 A Cont of US 5256767; US 5928930 A Cont of US 5256767, Div ex US 5853725; US 6017543 A Cont of US 5256767
PRAI US 1988-200752 19880531; US 1987-60280 19870610; US 1992-975899 19921110; BR 1997-1101124 19970514; US 1993-121318 19930915; US 1994-233508 19940426; US 1995-469739 19950605; US 1995-467334 19950605; US 1995-464139 19950605; US 1995-464137 19950605; US 1995-467302 19950605

AB WO 8809670 A UPAB: 19970926
The following are claimed: (a) an immunogen comprising non-infectious retroviral particles devoid of outer envelope proteins, (b) a method of stimulating the immune system of a human having a retrovirus infection by administering an immunogen comprising a non-infectious prepn. of the retrovirus, (c) a method of preventing HIV infection in a human by administering a non-infectious outer-envelope-free prepn. of HIV, (d) antibodies reactive with one or more retroviral proteins but not reactive with the outer envelope proteins of the retrovirus, (e) a method of obtaining immunoglobulins useful for the treatment of retroviral infections comprising (i) selecting an individual having a retroviral infection and exhibiting high immunocompetence and (ii) recovering immunoglobulins produced by the individual; (f) a method for the extracorporeal removal of antibodies to gp. 160/120 from an individual infected with HIV comprising (i) extracorporeally contacting blood from the individual with a matrix to which are attached ligands reactive with gp.160/120 such that antibodies to gp.160/210 will bind to the matrix and (ii) returning the blood to the patient, and (g) anti-idiotype antibodies reactive with anti-gp.160/210 antibodies.
USE - The methods and agents can be used in the prevention and therapy of retroviral infections, partic. HIV.
Dwg.0/4

L18 ANSWER 18 OF 18 MEDLINE on STN

97265570 Document Number: 97265570. PubMed ID: 9111476. Effect of immunization with an inactivated gp120-depleted HIV-1 immunogen on beta-chemokine and cytokine production in subjects with HIV-1 infection. Moss R B; Trauger R J; Giermakowska W K; Turner J L; Wallace M R; Jensen F C; Richieri S P; Ferre F; Daigle A E; Duffy C; Theofan G; Carlo D J. (Immune Response Corporation, Carlsbad, California 92008, USA.) JOURNAL OF ACQUIRED IMMUNE DEFICIENCY SYNDROMES AND HUMAN RETROVIROLOGY, (1997 Apr 1) 14 (4) 343-50. Journal code: 9501482. ISSN: 1077-9450. Pub. country: United States. Language: English.

AB OBJECTIVE: To measure beta-chemokine and cytokine production in HIV-1-infected subjects undergoing treatment with HIV-1 immunogen (REMUNE). DESIGN: Open label treatment study. METHODS: beta-Chemokine and cytokine production in peripheral blood mononuclear cell (PBMC) culture. RESULTS: Interferon-gamma production ($p = 0.04$) and lymphocyte proliferation ($p = 0.001$) to HIV-1 antigen-stimulated PBMCs increased after immunization with the HIV-1 immunogen. A correlation was demonstrated after immunization between HIV-1 antigen-stimulated lymphocyte proliferation and interferon-gamma levels ($r = 0.53$, $p = 0.04$). No significant change after immunization was seen for interleukin-4 production. A significant increase in mean levels of HIV-1 antigen-stimulated RANTES (i.e., regulated upon, activation normal T-cell expressed and secreted), was evident 1 month after immunization ($p = 0.002$) and remained elevated 3 months after immunization. RANTES production was decreased in CD8-depleted PBMC cultures. Mean serum HIV-1 RNA copy numbers and CD4 cell counts remained stable after immunization ($p > 0.5$). A correlation was demonstrated between HIV-1 antigen-stimulated interferon-gamma and RANTES production ($r = 0.54$, $p = 0.002$). CONCLUSIONS: This report describes an augmentation of beta-chemokines and TH1-type cytokines from PBMCs after immunization with the HIV-1 immunogen.

L18 ANSWER 17 OF 18 MEDLINE on STN

1998132495 Document Number: 98132495. PubMed ID: 9473153. Cross-clade immune responses after immunization with a whole-killed gp120-depleted human immunodeficiency virus type-1 immunogen in incomplete Freund's adjuvant (HIV-1 immunogen, REMUNE) in human immunodeficiency virus type-1 seropositive subjects. Moss R B; Giermakowska W; Lanza P; Turner J L; Wallace M R; Jensen F C; Theofan G; Richieri S P; Carlo D J. (Immune Response Corporation, Carlsbad, California 92008, USA.) VIRAL IMMUNOLOGY, (1997) 10 (4) 221-8. Journal code: 8801552. ISSN: 0882-8245. Pub. country: United States. Language: English.

AB Lymphocyte proliferation responses to gp120-depleted HZ321 virus (clade A) antigen were compared to BAL human immunodeficiency virus (HIV) virus antigen (clade B) responses, clade E HIV virus antigen responses, and purified native p24 antigen responses in 15 human immunodeficiency virus type-1 (HIV-1) seropositive subjects immunized with a whole-killed inactivated gp120-depleted HIV-1 antigen in Incomplete Freund's adjuvant (HIV-1 immunogen, REMUNE). A significant increase in lymphocyte proliferation to HZ321 antigen was observed after immunization with the HIV-1 immunogen ($p = 0.02$). A strong association was demonstrated between the HIV-1 immunizing antigen, HZ321, and native p24 antigen responses ($r = 0.80$, $p < 0.0001$). Furthermore, a strong association in terms of proliferative responses was demonstrated between HZ321 virus (clade A) responses and BAL virus (clade B) ($r = 0.95$, $p < 0.0001$) and clade E virus antigen ($r = 0.92$, $p < 0.0001$). Proliferative responses to HIV antigens also correlated with baseline CD4 counts. Taken together, these results

support the specificity of immune responses induced by REMUNE (HIV-1 immunogen). The development of cross-reactive immune responses between clades and to the more conserved epitopes of the virus have implications in the development of therapeutic and prophylactic HIV vaccines.

L18 ANSWER 15 OF 18 MEDLINE on STN

1998269905 Document Number: 98269905. PubMed ID: 9607022. Safety and immunogenicity of REMUNE in HIV-infected Thai subjects. Limsuwan A; Churdboonchart V; Moss R B; Sirawaraporn W; Sutthent R; Smutharaks B; Glidden D; Trauger R; Theofan G; Carlo D. (Department of Pathobiology, Mahidol University, Bangkok, Thailand.) VACCINE, (1998 Jan-Feb) 16 (2-3) 142-9. Journal code: 8406899. ISSN: 0264-410X. Pub. country: ENGLAND: United Kingdom. Language: English.

AB The safety and immunogenicity of REMUNE, an HIV-specific immune based therapy for HIV infection, was evaluated in a cohort of 30 HIV infected subjects in Thailand. This therapy utilizes a gp120 depleted inactivated virus (HZ321), which exhibits a high degree of conservation with the core antigens of both type B' and E strains of HIV, the predominant Thailand isolates. The treatment was well tolerated, with no serious adverse events reported over the course of the 4-month trial. Treatment in which four doses were administered with REMUNE appeared to boost HIV-specific immune responses, with approximately 75% of the treated subjects demonstrating an increase in either the repertoire or the intensity of the serological response to HIV as measured by Western blot. CD4%, viral load, and weight remained stable over the course of the 4-month study relative to baseline values. Viral subtyping of this cohort revealed a predominance of type 'E'. These data suggest that REMUNE is safe and immunogenic in seropositive Thai subjects and supports further study of the therapeutic potential of REMUNE to treat HIV-1 infection.

L18 ANSWER 14 OF 18 MEDLINE on STN

1998335956 Document Number: 98335956. PubMed ID: 9672235. A primer on HIV type 1-specific immune function and REMUNE. Moss R B; Giermakowska W K; Savary J R; Theofan G; Daigle A E; Richieri S P; Jensen F C; Carlo D J. (The Immune Response Corporation, Carlsbad, California 92008, USA.) AIDS RESEARCH AND HUMAN RETROVIRUSES, (1998 Jun) 14 Suppl 2 S167-75. Ref: 76. Journal code: 8709376. ISSN: 0889-2229. Pub. country: United States. Language: English.

AB The ability to recognize HIV antigens is lost early in HIV-1 infection. Individuals with nonprogressive HIV disease have been observed to mount strong immune responses against the virus and have become a paradigm to emulate with immune-based therapies. Highly active antiviral drug therapy (HAART) has now become the standard of care for HIV-1-infected individuals. Because HIV-specific anergy occurs early in HIV infection, HAART initiated after primary infection may not reconstitute HIV-specific immune function. We have been investigating the effects of an immune-based therapy, called REMUNE, in HIV-1-seropositive individuals. REMUNE has been observed to stimulate HIV-1-specific immune function measured by delayed-type hypersensitivity, lymphocyte proliferation, Th1 cytokine, and beta-chemokine production. Multiple Phase II studies and a Phase III clinical end-point study are ongoing in thousands of seropositive individuals in order to test the clinical utility of REMUNE. The clinical testing of REMUNE and other promising immune-based therapies may provide additional treatment modalities useful in the chronic management of HIV-1.

L18 ANSWER 12 OF 18 MEDLINE on STN

1999211139 Document Number: 99211139. PubMed ID: 10195235. Tumor necrosis factor alpha and human immunodeficiency virus-specific functional immune responses after immunization with Gp120-depleted, inactivated HIV-1 in incomplete Freund's adjuvant (REMUNE) in HIV-1-seropositive subjects. Moss R B; Li L; Giermakowska W K; Lanza P; Turner J L; Wallace M R; Jensen F C; Richieri S P; Daigle A E; Theofan G; Carlo D J. (Immune Response Corporation, Carlsbad, California 92008, USA.) JOURNAL OF HUMAN VIROLOGY, (1998 Jan-Feb) 1 (2) 77-81. Journal code: 9805755. ISSN: 1090-9508. Pub. country: United States. Language: English.

AB OBJECTIVE: We examined the relation between tumor necrosis factor-alpha (TNF-alpha) levels and human immunodeficiency virus type 1 (HIV-1)-specific functional immune responses, as measured by HIV-1 antigen-stimulated lymphocyte proliferation and beta-chemokine production after immunization with gp120-depleted, inactivated HIV-1 in incomplete Freund's adjuvant (i.e., HIV-1 Immunogen; REMUNE, The Immune Response Corporation, Carlsbad, CA, U.S.A.). STUDY DESIGN/METHODS: HIV-1-seropositive subjects who enrolled in an open-label study were immunized with REMUNE every 12 weeks and monitored for 60 weeks. HIV-1 antigen-stimulated lymphocyte proliferation and RANTES production were measured in peripheral blood mononuclear cells (PBMCs). TNF-alpha levels were measured in serum. RESULTS: TNF-alpha ($P = 0.0003$) significantly decreased and HIV-1 antigen-stimulated RANTES production ($P = 0.002$) and lymphocyte proliferation ($P = 0.07$) increased after immunization with REMUNE. TNF-alpha levels negatively correlated with HIV-1 antigen-stimulated RANTES production ($r = -0.71$; $P = 0.0002$) and lymphocyte proliferation ($r = -0.37$; $P = 0.09$). CONCLUSIONS: This study demonstrated decreased TNF-alpha levels with a concomitant augmentation of HIV-specific functional immunity in subjects immunized with REMUNE. Because TNF-alpha has been implicated in the induction of anergy in HIV-1 infection, the ability to decrease TNF-alpha may allow the immune system to respond to HIV and non-HIV antigens. Larger studies are being conducted to confirm the clinical utility of REMUNE in combination with potent antiviral drugs.

L18 ANSWER 13 OF 18 MEDLINE on STN

1998394557 Document Number: 98394557. PubMed ID: 9727574. Effect of HIV-specific immune-based therapy in subjects infected with HIV-1 subtype E in Thailand. Churdboonchart V; Moss R B; Sirawaraporn W; Smutharaks B; Sutthent R; Jensen F C; Vacharak P; Grimes J; Theofan G; Carlo D J. (Mahidol University, Phayathai, Bangkok, Thailand.) AIDS, (1998 Aug 20) 12 (12) 1521-7. Journal code: 8710219. ISSN: 0269-9370. Pub. country: United States. Language: English.

AB OBJECTIVE: To examine the effect of treatment with an inactivated, gp120-depleted, HIV-1 immunogen (Remune) in 30 Thai subjects infected with HIV-1 subtype E. DESIGN: Sixty-week open-label study. METHODS: Thirty HIV-positive volunteers with CD4 cell counts > or = 300 x 10(6)/l were given intramuscular injections of Remune into the triceps muscle on day 1 and then at weeks 4, 8, 12, 24, 36, 48 and 60. RESULTS: Treatment with Remune was well-tolerated and augmented HIV-1-specific immune responses. Furthermore, subjects had a significant increase in CD4 cell count ($P < 0.0001$), CD4 cell percentage ($P < 0.0001$), CD8 cell percentage ($P < 0.0001$), and body weight ($P < 0.0001$) compared with pretreatment levels. Fourteen subjects with detectable viral load at day 1 showed a decrease at week 60 ($P=0.04$). Retrospective Western blot analysis showed 23 subjects with increased intensity of antibody bands and 15 patients showed development of new reactivities to HIV proteins, especially towards p17 and p15. CONCLUSION: These results indicate that HIV-specific immune-based therapeutic approaches such as Remune should be further

examined in countries with different clades of HIV-1 and where access to antiviral drug therapies is limited.

L18 ANSWER 11 OF 18 MEDLINE on STN

1999367568 Document Number: 99367568. PubMed ID: 10438350. Phenotypic analysis of human immunodeficiency virus (HIV) type 1 cell-mediated immune responses after treatment with an HIV-1 immunogen. Moss R B; Wallace M R; Giermakowska W K; Webb E; Savary J; Chamberlin-Brandt C; Theofan G; Musil R; Richieri S P; Jensen F C; Carlo D J. (Immune Response Corp., Carlsbad, CA 92008, USA.. shotdoc@imnr.com) . JOURNAL OF INFECTIOUS DISEASES, (1999 Sep) 180 (3) 641-8. Journal code: 0413675. ISSN: 0022-1899. Pub. country: United States. Language: English.

AB It was hypothesized that immune recognition could be stimulated with combined immune-based and potent antiviral drug therapies. This study examined human immunodeficiency virus type 1 (HIV-1)-specific lymphocyte proliferation before and after treatment with an inactivated HIV-1 immunogen in 15 chronically infected HIV-1 seropositive subjects. Lymphocyte proliferation to the immunizing antigen (gp120-depleted HIV-1; P<.001), purified native p24 (P<.001), and recombinant p24 (P<.05) increased after treatment with the HIV-specific immune-based therapy. By HIV-1 antigen-specific flow cytometry, T helper CD4 lymphocytes, CD8 lymphocytes, and NK cells (all P<.001) were the predominant cell types proliferating in vitro after treatment. Additional phenotyping of proliferating cells revealed predominantly CD4 and CD8 memory (both P<.001) phenotypes. This study supports the concept that in vitro lymphocyte proliferation to HIV-1 antigens, augmented after treatment with an inactivated HIV-1 immunogen, involves primarily CD4 and CD8 cell memory immune responses.

L18 ANSWER 10 OF 18 MEDLINE on STN

1999437259 Document Number: 99437259. PubMed ID: 10509560. **Cell-associated HIV-1 messenger RNA and DNA in T-helper cell and monocytes in asymptomatic HIV-1-infected subjects on HAART plus an inactivated HIV-1 immunogen. Patterson B K; Carlo D J; Kaplan M H; Marecki M; Pawha S; Moss R B. (Northwestern University Medical School, Department of Obstetrics/Gynecology and Medicine, Chicago, Illinois 60611, USA.. bpatters@nmh.org) . AIDS, (1999 Sep 10) 13 (13) 1607-11.** Journal code: 8710219. ISSN: 0269-9370. Pub. country: ENGLAND: United Kingdom. Language: English.

AB OBJECTIVE: We examined the effect of an HIV-1-specific immune-based therapy on cell-associated HIV-1 DNA and RNA. DESIGN: **Five HIV-1-infected subjects receiving HIV-1 immunogen plus HAART were compared with three HIV-1-infected subjects who received incomplete Freund's adjuvant (IFA) plus HAART.** METHODS: Cell-associated HIV-1 RNA or DNA in lymphocytes and monocytes was determined using a dual immunophenotyping/in situ hybridization assay with or without in situ PCR amplification. RESULTS: Cell-associated HIV-1 RNA in CD4 cells correlated with plasma RNA overall. CD4, HIV-1 gag-pol messenger (m)RNA+ cells decreased in the immunogen plus HAART group compared with the IFA plus HAART group. Decreases in HIV-1 DNA+ CD4 cells were observed in the immunogen plus HAART compared with the IFA plus HAART group. Decreases in HIV-1 gag-pol mRNA+ monocytes were observed in the immunogen plus HAART group compared with the IFA plus HAART group. Consistent with the findings in CD4 cells, decreases in HIV-1 DNA+ monocytes were observed in the immunogen plus HAART group compared with the IFA plus HAART group. CONCLUSIONS: **These preliminary observations support the rationale for examining the combination of**

immune-based therapies and antiretroviral drugs for effective HIV-1 control.

L18 ANSWER 7 OF 18 MEDLINE on STN

2000456899 Document Number: 20429905. PubMed ID: 10969351. **HIV-1-Specific CD4 helper function in persons with chronic HIV-1 infection on antiviral drug therapy as measured by ELISPOT after treatment with an inactivated, gp120-depleted HIV-1 in incomplete Freund's adjuvant. Moss R B; Webb E; Giermakowska W K; Jensen F C; Savary J R; Wallace M R; Carlo D J. (The Immune Response Corporation, Carlsbad, California 92008, USA.. shotdoc@imnr.com) . JOURNAL OF ACQUIRED IMMUNE DEFICIENCY SYNDROMES, (2000 Jul 1) 24 (3) 264-9.** Journal code: 100892005. ISSN: 1525-4135. Pub. country: United States. Language: English.

AB OBJECTIVE: We hypothesized that treatment of HIV-1-seropositive study subjects receiving potent antiviral therapy with an HIV-specific immune-based therapy would increase HIV-1-specific T-helper immune function. DESIGN: **10 HIV-1-seropositive study subjects receiving antiretroviral therapy were treated with an inactivated, gp120-depleted immunogen in IFA (HIV-1 immunogen, Remune) at baseline, week 12, and week 24.** METHODS: The frequency of HIV-1 antigen-stimulated interferon-gamma (IFN-gamma)-producing cells was determined by the ELISPOT assay. RESULTS: Study subjects significantly increased their frequency of HIV-1-stimulated ($p < .001$) or p24 antigen-stimulated ($p < .01$) IFN-gamma-producing cells after one, two, and three treatments of HIV-1 immunogen. Depletion of CD4 cells resulted in the strongest abrogation of the IFN-gamma response. The frequency of HIV-1 ($r = 0.64$; $p = .0002$) and p24 ($r = 0.72$; $p < .001$) antigen-stimulated IFN-gamma-producing cells in the CD8-depleted population before and after treatment was associated with the lymphocyte-proliferative response. CONCLUSIONS: Treatment with HIV-1 immunogen significantly enhanced the frequency of HIV-1-specific IFN-gamma-producing cells. Studies are ongoing to determine the relationship between this reversal of HIV-specific anergy and virologic outcomes.

L18 ANSWER 6 OF 18 MEDLINE on STN

2001010074 Document Number: 20429443. PubMed ID: 10973444. **T-helper-cell proliferative responses to whole-killed human immunodeficiency virus type 1 (HIV-1) and p24 antigens of different clades in HIV-1-infected subjects vaccinated with HIV-1 immunogen (Remune). Moss R B; Giermakowska W; Wallace M R; Savary J; Jensen F; Carlo D J. (The Immune Response Corporation, Carlsbad, California 92008, USA.. shotdoc@imnr.com) . CLINICAL AND DIAGNOSTIC LABORATORY IMMUNOLOGY, (2000 Sep) 7 (5) 724-7.** Journal code: 9421292. ISSN: 1071-412X. Pub. country: United States. Language: English.

AB The discovery of multiple subtypes of human immunodeficiency virus type 1 (HIV-1) worldwide has created new challenges for the development of both therapeutic and preventive AIDS vaccines. We examined T-helper proliferative responses to HIV-1 clade A, B, C, G, and E whole-killed virus and to HIV-1 clade G and B core (p24) antigens in **HIV-1-infected subjects taking potent antiviral drugs who received HIV immunogen (Remune) therapeutic vaccination.** Subjects who were immunized mounted strong proliferative responses to both whole virus and core antigens of the different clades. These results suggest that a whole-killed immunogen may have broad applications as a therapeutic as well as a preventive vaccine in the current multiclade HIV-1 pandemic.